PATENT
Attorney Docket No. **HOGAN-06650**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Kirk Hogan		
Serial No.:	09/976,423	Group No.:	1634
Filed:	10/12/01	Examiner:	Goldberg
Entitled:	**Methods and Compositions for Perioperative Genomic Profiling**		

TRANSMITTAL OF APPEAL BRIEF (PATENT APPLICATION - 37 CFR§ 192)

Mail Stop Appeal Brief - Patents
Commissioner for Patents
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Dated: November 7, 2005 By: _____
Mary Ellen Waite

Sir or Madam:

1. Transmitted herewith, in triplicate, is the APPEAL BRIEF in this application, with respect to the Notice of Appeal filed on **11/07/2005**.

2. **STATUS OF APPLICANT**

This application is on behalf of

a small entity.

A verified statement has already been filed.

3. **FEE FOR FILING APPEAL BRIEF**

Pursuant to 37 CFR § 1.17(g), the fee for filing the Appeal Brief is:

Fee for Filing Appeal Brief $250.00

3. **NOTICE OF APPEAL**

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4. **EXTENSION OF TERM**

The proceedings herein are for a patent application and the provisions of 37 CFR § 1.136 apply.

Applicant petitions for a three month extension of time under 37 CFR § 1.136 (fees: 37 CFR §§1.17(a)-(d)).

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02 FC:2402 250.00 OP

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6. **FEE PAYMENT**

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7. **FEE DEFICIENCY**

If any additional fee is required, charge Account No. **08-1290**.

Dated: November 7, 2005

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Kirk Hogan		
Serial No.:	09/976,423	Group No.:	1634
Filed:	10/21/2001	Examiner:	J.A. Goldberg
Entitled:	Methods and Compositions for Perioperative Genomic Profiling		

APPELLANT'S BRIEF

APPEAL NO.:

CERTIFICATE OF FACSIMILE TRANSMISSION UNDER 37 C.F.R. § 1.8(a)(1)(i)(B)

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11-7-05

By: Mary Ellen Waite

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Madam/Sir:

This Brief is in furtherance of the Notice of Appeal mailed herewith.

The fees required under SS 1.17(h) and any required Petition for Extension of time for filing this Brief and fees therefore are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

This Brief is transmitted in triplicate. [37 CFR § 1.192(a).]

This Brief contains these items under the following headings and in the order set forth below [37 CFR § 1.192(c)]:

I. REAL PARTY IN INTEREST

The real party in interest is the inventor of record, Kirk Hogan.

II. RELATED APPEALS AND INTERFERENCES

U.S. patent application No. 09/613,887, filed July 11, 2000, is under appeal and may be related to the pending appeal.

III. STATUS OF CLAIMS

Claims 1-23 were filed in the original application. During prosecution of the application, Claims 1-23 were canceled and Claims 24-44 were added in the Amendment and Response to Office Action filed January 8, 2003. Claims 24-44 were canceled and Claims 45-71 were added in the Amendment and Response to Office Action filed May 23, 2003. Claims 69 and 70 were canceled in the Amendment and Response to Final Office Action filed June 30, 2004. Claims 45-68, and 71 were canceled, and Claims 72-107 were added in the Amendment and Response to Office Action filed February 14, 2005. Claims 72-107 have been rejected by the Office in the Final Office Action dated May 10, 2005. No other Claims are pending. Therefore, Claims 72-107 are pending in this appeal. The Appellant appeals the Final Office Action of May 10, 2005.

The Claims, as they now stand, are set forth in Section VIII. CLAIMS APPENDIX.

IV. STATUS OF AMENDMENTS

All previous amendments have been entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention relates to kits for perioperative genomic screening of surgical subjects. In some embodiments, the present invention relates to kits for perioperative genomic screening for nucleic acid genetic markers indicative of responses to anesthesia, and to other perioperative or operative treatments and procedures, comprising, for example, reagents sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the

group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*.

In current clinical practice, there is no technology available that provides the information of the kits for generating perioperative genomic profiles of the present invention. In the past, screening tests of a patient's phenotype (*e.g.*, blood cell count and chemistries, urinalysis, electrocardiogram (EKG), and chest X-ray) were routinely performed prior to surgery. However, the present-day procedure for screening for susceptibility to heritable disorders of consequence in the interval surrounding surgery does not look at nucleic acid genetic markers, and is limited to asking a patient if they or their family members have had any previous difficulties with anesthesia or surgery. The use of laboratory phenotypic tests for patients prior to surgery has generally been reduced or eliminated. The reasons for elimination include the inaccuracy and lack of specificity of the various phenotypic tests, the aggregate costs of many different kinds of phenotypic screening tests necessary to assemble test panels, and uncertainty as to how to alter a treatment course of action in response to phenotypic test results. Accordingly, contemporary anesthesiology and surgery textbooks emphasize that recent studies indicate a lack of benefit from phenotypic testing as a method of assessing patients before surgery, and stress that cost-benefit strategies can only be justified when laboratory testing is reduced to that indicated by history-taking.

The kits for generating perioperative genomic profiles of the present invention stand in direct contrast to the history-taking and panels of phenotypic tests currently available and previously used. In the present invention, genetic alleles are tested in ensemble according to selection categories and criteria taught by the present invention, in order to construct a personalized perioperative genomic profile. The kits for generating perioperative genomic profiles of the present invention may be used, for example, to select the safest and most effective anesthetic regimen and surgical procedure, and to begin life-saving interventions as soon as possible. The kits for generating perioperative genomic profiles of the present invention thereby solve many of the problems described above that have led practitioners away from preoperative phenotypic testing. The kits for generating perioperative genomic profiles of the present invention are cost and time effective. As taught by the present invention, genomic markers are selected for inclusion

in the profile by virtue of their analytical validity (*i.e.*, a high level of accuracy, specificity, and predictive value), their clinical validity (*i.e.*, a high level of correlation between DNA sequence variation and the trait of interest), and their clinical utility (*i.e.*, a significant impact of the test result on the patient's well-being during and after surgery). The kits for generating perioperative genomic profiles of the present invention thus allow for the individualization of treatment options for each subject undergoing a surgical procedure. In this fashion, the present invention provides a novel diagnostic tool currently unavailable in the surgical field, enabling solutions for problems that have no available alternatives. In the absence of any competing technology for quantifying subject's genetic contributors to perioperative risk, the present invention provides time-, cost-, and life-saving information to caregivers on an accelerated and amplified scale relative to current diagnostics.

In one embodiment of the present invention, a kit (described, for example, in the Specification at page 6, lines 15 – 20) for generating a perioperative genomic profile (described, for example, at page 3, lines 29 - 30, page 4, lines 7 - 12, page 18, lines 26 - 27, page 5, line 20, page 6, lines 15 - 20, page 8, lines 1 - 2, and lines 10 - 11, page 27, lines 13 – 17, and Figure 5) for a subject (described, for example, at page 29, lines 12 - 14), said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure (described, for example, at page 25, lines 25 - 30) is described, comprising reagents (described, for example, at page 6, lines 20 - 21, page 19, lines 23 - 27, page 41, lines 4 - 5, page 45, lines 24 - 29, page 46, line 2, page 54, lines 27 - 28, and page 40, line 25 – page 49, line 2, "Assays for Generating Genomic Profiles") configured such that when exposed to a sample (described, for example, at page 29, line 4 – 11) containing target nucleic acid (described, for example, at page 11, lines 4 – 23) from a perioperative subject, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions (described, for example, at Figure 4 "Allele Panel", and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers") selected from the group consisting of *BChE* (described, for example, at page 6, lines 21 – 22), *CYP2D6* (described, for example, at page 6, lines 22 – 24), *F5* (described, for example, at page 6, lines 28 – 29), *F2* (described, for example, at page 6, line 2), *CACNAIS* (described, for

example, at page 7, lines 1 – 2), *MTHFR* (described, for example, at page 6, line 26), *MTR* (described, for example, at page 6, lines 26 – 27), *CBS* (described, for example, at page 6 lines 27 – 28), *TNFα* (described, for example, at page 7, lines 3 – 4), and *TNFβ* (described, for example, at page 7, line 4) (and described, for example, in Figure 5 "Detection of Allelic Variants"), so as to generate a genomic profile for use in selecting a perioperative course of action for said subject (described, for example, at page 3, line 30 – page 4, line 2, page 28, lines 9 – 13 and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers"), and a computer program (described, for example, at page 40, line 29 – page 41, line 5, page 49, lines 4 - 12 "Computer-Based Data Analysis", and page 50, lines 8 – 12), comprising instructions (described, for example, at page 6, lines 19 – 20) which direct a processor (described, for example, at page 50, line 19 – page 51, line 7) to analyze data derived from use of said reagents (described, for example, at page 49, line 14 – page 53, line 3, "Analysis and Delivery of Data").

In another embodiment of the present invention, a kit (described, for example, in the Specification at page 6, lines 15 – 20) for generating a perioperative genomic profile (described, for example, at page 3, lines 29 - 30, page 4, lines 7 - 12, page 18, lines 26 - 27, page 5, line 20, page 6, lines 15 - 20, page 8, lines 1 - 2, and lines 10 - 11, page 27, lines 13 – 17, and Figure 5) for a subject (described, for example, at page 29, lines 12 - 14), said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure (described, for example, at page 25, lines 25 - 30) is described, comprising reagents (described, for example, at page 6, lines 20 - 21, page 19, lines 23 - 27, page 41, lines 4 - 5, page 45, lines 24 - 29, page 46, line 2, page 54, lines 27 - 28, and page 40, line 25 – page 49, line 2, "Assays for Generating Genomic Profiles") configured such that when exposed to a sample (described, for example, at page 29, line 4 – 11) containing target nucleic acid (described, for example, at page 11, lines 4 – 23) from a perioperative subject, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions (described, for example, at Figure 4 "Allele Panel", and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers") selected from the group consisting of *BChE* (described, for example, at page 6, lines 21 – 22), *CYP2D6*

(described, for example, at page 6, lines 22 – 24), *F5* (described, for example, at page 6, lines 28 – 29), *F2* (described, for example, at page 6, line 2), *CACNAIS* (described, for example, at page 7, lines 1 – 2), *MTHFR* (described, for example, at page 6, line 26), *MTR* (described, for example, at page 6, lines 26 – 27), *CBS* (described, for example, at page 6 lines 27 – 28), *TNFα* (described, for example, at page 7, lines 3 – 4), and *TNFβ* (described, for example, at page 7, line 4) (and described, for example, in Figure 5 "Detection of Allelic Variants"), so as to generate a genomic profile for use in selecting a perioperative course of action for said subject (described, for example, at page 3, line 30 – page 4, line 2, page 28, lines 9 – 13 and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers"), and a computer program (described, for example, at page 40, line 29 – page 41, line 5, page 49, lines 4 - 12 "Computer-Based Data Analysis", and page 50, lines 8 – 12), comprising instructions (described, for example, at page 6, lines 19 – 20) which direct a processor (described, for example, at page 50, line 19 – page 51, line 7) to analyze data derived from use of said reagents (described, for example, at page 49, line 14 – page 53, line 3, "Analysis and Delivery of Data") to indicate an anesthesia treatment course of action (described, for example, at page 5, lines 7 - 8, page 6, lines 9 – 14).

In a further embodiment of the present invention, a kit (described, for example, in the Specification at page 6, lines 15 – 20) for generating a perioperative genomic profile (described, for example, at page 3, lines 29 - 30, page 4, lines 7 - 12, page 18, lines 26 - 27, page 5, line 20, page 6, lines 15 - 20, page 8, lines 1 - 2, and lines 10 - 11, page 27, lines 13 – 17, and Figure 5) for a subject (described, for example, at page 29, lines 12 - 14), said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure (described, for example, at page 25, lines 25 - 30) is described, comprising reagents (described, for example, at page 6, lines 20 - 21, page 19, lines 23 - 27, page 41, lines 4 - 5, page 45, lines 24 - 29, page 46, line 2, page 54, lines 27 - 28, and page 40, line 25 – page 49, line 2, "Assays for Generating Genomic Profiles") configured such that when exposed to a sample (described, for example, at page 29, line 4 – 11) containing target nucleic acid (described, for example, at page 11, lines 4 – 23) from a perioperative subject, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions (described, for

example, at Figure 4 "Allele Panel", and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers") selected from the group consisting of *BChE* (described, for example, at page 6, lines 21 – 22), *CYP2D6* (described, for example, at page 6, lines 22 – 24), *F5* (described, for example, at page 6, lines 28 – 29), *F2* (described, for example, at page 6, line 2), *CACNAIS* (described, for example, at page 7, lines 1 – 2), *MTHFR* (described, for example, at page 6, line 26), *MTR* (described, for example, at page 6, lines 26 – 27), *CBS* (described, for example, at page 6 lines 27 – 28), *TNFα* (described, for example, at page 7, lines 3 – 4), and *TNFβ* (described, for example, at page 7, line 4) (and described, for example, in Figure 5 "Detection of Allelic Variants"), so as to generate a genomic profile for use in selecting a perioperative course of action for said subject (described, for example, at page 3, line 30 – page 4, line 2, page 28, lines 9 – 13 and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers"), and a computer program (described, for example, at page 40, line 29 – page 41, line 5, page 49, lines 4 - 12 "Computer-Based Data Analysis", and page 50, lines 8 – 12), comprising instructions (described, for example, at page 6, lines 19 – 20) which direct a processor (described, for example, at page 50, line 19 – page 51, line 7) to analyze data derived from use of said reagents (described, for example, at page 49, line 14 – page 53, line 3, "Analysis and Delivery of Data") to indicate a surgical treatment course of action (described, for example, at page 3, lines 19 - 30, page 4, lines 22 - 23, page 6, lines 23 - 24, and page 9, lines 27 – 28).

In an additional embodiment of the present invention, a perioperative genomic profile (described, for example in the Specification, at page 3, lines 29 - 30, page 4, lines 7 - 12, page 18, lines 26 - 27, page 5, line 20, page 6, lines 15 - 20, page 8, lines 1 - 2, and lines 10 - 11, page 27, lines 13 – 17, and Figure 5) kit is described (described, for example, at page 6, lines 15 – 20) having component parts (described for example at page 19, lines 25 – 27, page 25, lines 21 – 24, and page 58, lines 16 –25)configured such that when exposed to a sample (described, for example, at page 29, line 4 – 11) containing target nucleic acid (described, for example, at page 11, lines 4 – 23) from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure (described, for example, at page 25, lines 25 - 30), are

sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions (described, for example, at Figure 4 "Allele Panel", and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers") selected from the group consisting of *BChE* (described, for example, at page 6, lines 21 – 22), *CYP2D6* (described, for example, at page 6, lines 22 – 24), *F5* (described, for example, at page 6, lines 28 – 29), *F2* (described, for example, at page 6, line 2), *CACNAIS* (described, for example, at page 7, lines 1 – 2), *MTHFR* (described, for example, at page 6, line 26), *MTR* (described, for example, at page 6, lines 26 – 27), *CBS* (described, for example, at page 6 lines 27 – 28), *TNFα* (described, for example, at page 7, lines 3 – 4), and *TNFβ* (described, for example, at page 7, line 4) (and described, for example, in Figure 5 "Detection of Allelic Variants") to generate a genomic profile (described, for example, at page 3, lines 29 - 30, page 4, lines 7 - 12, page 18, lines 26 - 27, page 5, line 20, page 6, lines 15 - 20, page 8, lines 1 - 2, and lines 10 - 11, page 27, lines 13 – 17, and Figure 5) for use in selecting a perioperative course of action for said subject (described, for example, at page 3, line 30 – page 4, line 2, page 28, lines 9 – 13 and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers"), and thereby providing a subject-specific clinical pathway for said subject (described for example in Figure 1 "Alter Intervention" and Figure 3 "Therapeutic Plan"), comprising information to optimize perioperative care that, based at least on the presence or absence of are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions (described, for example, at Figure 4 "Allele Panel", and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers") selected from the group consisting of *BChE* (described, for example, at page 6, lines 21 – 22), *CYP2D6* (described, for example, at page 6, lines 22 – 24), *F5* (described, for example, at page 6, lines 28 – 29), *F2* (described, for example, at page 6, line 2), *CACNAIS* (described, for example, at page 7, lines 1 – 2), *MTHFR* (described, for example, at page 6, line 26), *MTR* (described, for example, at page 6, lines 26 – 27), *CBS* (described, for example, at page 6 lines 27 – 28), *TNFα* (described, for example, at page 7, lines 3 – 4), and *TNFβ* (described, for example, at page 7, line 4) (and described, for example, in Figure 5 "Detection of Allelic Variants") directs a user (described, for example, in Figure 1 "MD User Interpretation"

and at page 10, lines 17 – 20, page 50, lines 8 – 18, page 50, line 19 – page 53, line 3, and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers"), to a specific clinical pathway of medical intervention for said subject (described, for example, at page 4, lines 16 – 24 and page 5, lines 4 - 6.)

In one embodiment of the present invention, a perioperative genomic profile (described, for example in the Specification, at page 3, lines 29 - 30, page 4, lines 7 - 12, page 18, lines 26 - 27, page 5, line 20, page 6, lines 15 - 20, page 8, lines 1 - 2, and lines 10 - 11, page 27, lines 13 – 17, and Figure 5) kit is described (described, for example, at page 6, lines 15 – 20) having component parts (described for example at page 19, lines 25 – 27, page 25, lines 21 – 24, and page 58, lines 16 –25)configured such that when exposed to a sample (described, for example, at page 29, line 4 – 11) containing target nucleic acid (described, for example, at page 11, lines 4 – 23) from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure (described, for example, at page 25, lines 25 - 30), are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions (described, for example, at Figure 4 "Allele Panel", and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers") selected from the group consisting of *BChE* (described, for example, at page 6, lines 21 – 22), *CYP2D6* (described, for example, at page 6, lines 22 – 24), *F5* (described, for example, at page 6, lines 28 – 29), *F2* (described, for example, at page 6, line 2), *CACNAIS* (described, for example, at page 7, lines 1 – 2), *MTHFR* (described, for example, at page 6, line 26), *MTR* (described, for example, at page 6, lines 26 – 27), *CBS* (described, for example, at page 6 lines 27 – 28), *TNFα* (described, for example, at page 7, lines 3 – 4), and *TNFβ* (described, for example, at page 7, line 4) (and described, for example, in Figure 5 "Detection of Allelic Variants") to generate a genomic profile (described, for example, at page 3, lines 29 - 30, page 4, lines 7 - 12, page 18, lines 26 - 27, page 5, line 20, page 6, lines 15 - 20, page 8, lines 1 - 2, and lines 10 - 11, page 27, lines 13 – 17, and Figure 5) for use in selecting a perioperative course of action for said subject (described, for example, at page 3, line 30 – page 4, line 2, page 28, lines 9 – 13 and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers"), and thereby providing a subject-specific clinical pathway for said subject

(described for example in Figure 1 "Alter Intervention" and Figure 3 "Therapeutic Plan"), comprising information to optimize perioperative care that, based at least on the presence or absence of are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions (described, for example, at Figure 4 "Allele Panel", and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers") selected from the group consisting of *BChE* (described, for example, at page 6, lines 21 – 22), *CYP2D6* (described, for example, at page 6, lines 22 – 24), *F5* (described, for example, at page 6, lines 28 – 29), *F2* (described, for example, at page 6, line 2), *CACNAIS* (described, for example, at page 7, lines 1 – 2), *MTHFR* (described, for example, at page 6, line 26), *MTR* (described, for example, at page 6, lines 26 – 27), *CBS* (described, for example, at page 6 lines 27 – 28), *TNFα* (described, for example, at page 7, lines 3 – 4), and *TNFβ* (described, for example, at page 7, line 4) (and described, for example, in Figure 5 "Detection of Allelic Variants") directs a user (described, for example, in Figure 1 "MD User Interpretation" and at page 10, lines 17 – 20, page 50, lines 8 – 18, page 50, line 19 – page 53, line 3, and page 35, line 22 – page 40, line 4, "Applications and Interventions for Specific Markers"), to a specific clinical pathway of anesthesia intervention for said subject (described, for example, at page 4, line 24 – page 5, line 3, and page 5, lines 6 – 8).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

There are two grounds of rejection to be reviewed in the present appeal:

Ground of rejection 1 – Whether Claims 72-107 contain subject matter that was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention; and

Ground of rejection 2 – Whether Claims 72-107 are anticipated by the 1993 Applied Biosystems Product Catalog, pages 135-164.

VII. ARGUMENT

A. Ground of Rejection 1 – The Specification Fully Supports the Subject Matter of Claims 72-107

1. The Specification Fully Supports the Subject Matter of Claims 72-105

In the Final Office Action of May 10, 2005 the Examiner argues:

"Claims 72-107 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, reference to "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents" are (sic) included. The amendment fails to propose the basis for the new claim. Upon review by the examiner of support for the newly added recitation, the specification does not describe or discuss "a computer program comprising instructions which direct a processor to analyze data from use of said reagents." (Final Office Action of May 10, 2005, pages 2-3.)

And:

"The specification fails to teach a kit comprises (sic) each of these components. There is no disclosure in the instant specification of a kit comprising reagents and a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents." (Final Office Action of May 10, 2005, page 3.)

The Examiner is mistaken. First, Claims 106 and 107 do not include a reference to "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents".

Second, and contrary to the Examiner's assertion, the Specification provides full, specific and easily understood support for Claims 72-105. For example:

> "Once the particular SNPs and mutations have been determined for a given perioperative genomic panel, a profile is generated. Genomic profiles are generated through the detection of SNPs and mutations in a DNA sample (*e.g.*, a tissue sample or genetic information sample) from a subject. Assays for detections polymorphisms or mutations fall into several categories, including, but not limited to direct sequencing assays, fragment polymorphism assays, hybridization assays, and computer based data analysis. Protocols and commercially available kits or services for performing multiple variations of these assays are available." (Specification, page 40, line 25 – page 41, line 5.) (Emphasis added.)

And:

> "In some embodiments, the present invention provides a kit for generating a perioperative genomic profile for a subject, comprising a reagent capable of detecting the presence of a variant allele of two or more genetic markers selected from the group consisting of BChE, P450CYP2D6, F 5 Leiden, Prothrombin FII, RYR1, CACNA1S, MTHFR, MTRR, CBS, TNFα and TNFβ, and instructions for using the kit for generating the perioperative genomic profile for the subject." (Specification, page 6, lines 15 – 20.) (Emphasis added.)

And:

> "In some embodiments, a computer-based analysis program is used to translate raw data generated by the genomic profile (e.g., the presence or absence of a given SNP or mutation) into data of predictive value for the clinician (e.g., a probability of abnormal

pharmacological response, presence of an underlying disease, or differential diagnosis of known disease). (Specification, page 50, lines 8 – 12.) (Emphasis added.)

Hence, the Specification provides explicit teachings for each term of the claim element in question i.e., "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents". With regard to "a computer program comprising instructions", a computer program is defined as:

"A "computer program" is a set of statements or instructions to be used directly or indirectly in a computer in order to bring about a certain result." (U.S. Code Title 17, Chapter 1, §101.) (Emphasis added.)

And:

"program, *Computers*. the precise sequence of instructions enabling a computer to solve a problem." (Random House Unabridged Dictionary, 1997.) (Italics original, emphasis added.)

In turn, a "processor" is defined as:

"**processor**, 2 a (1): **COMPUTER b**: a computer program (as a compiler) that puts another program into a form acceptable to the computer." (Merriam Webster Dictionary.) (Emphasis and underlining in original.)

And:

"computer, **1**. Also called **processor**." (Random House Unabridged Dictionary, 1997.) (Emphasis in original.)

Similarly, copious support for "data derived from use of said reagents" is found in the Specification at, for example, "Detailed Description of the Invention", Section I. "Selection of

Markers for Genomic Profile", Subsection D. "Applications and Interventions of Specific Markers", Specification, page 35, line 22 – page 40, line 4 and **Subsection E. "Computer-Based Data Analysis"**, Specification, page 49, lines 4 - 12.

The Examiner argues:

> "With respect to paragraph 188, there is no teachings (sic) of a computer program within kit. Further, there is no teachings (sic) of a computer program comprising instructions which direct a processor to analyze data derived from the use of said reagents." (Final Office Action of May 10, 2005, page 4.)

The Examiner is in error. To the contrary, The Patent and Trademark Office's Final Office Action of May 10, 2005 fails to point out which components are believed by the Examiner to be lacking in the Specification in support of the element "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents". All claims of the present invention are drawn to kits that are expressly taught in the Specification (see above). The "computer program", the "instructions", the "processor" ("computer"), the "data", and the "reagents" of the claim element in question are explicitly and abundantly disclosed in the Specification, as is the data analysis step.

Moreover, adequate description under 35 U.S.C. §112, first paragraph, does not require verbatim support in the Specification for the claimed invention. It is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that the Appellant had possession of the concept of what is claimed.[1] Similarly, citing longstanding precedent, the Federal Circuit has recently held that *in haec verba* support in the Specification is not required: "In order to comply with the written description requirement, the specification 'need not describe the claimed subject matter in exactly the same terms as used in the claims; it must simply indicate to persons skilled in the art that as of the [filing] date the applicant had invented what is now claimed.' *Eiselstein v. Frank*, F.3d 1035, 1038, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995) (citing *Vas-Cath*, 935 F.2d at 1562, 19 USPQ2d at

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[1] *Ex parte Parks*, 30 USPQ 2d 1234 (B.P.A.I. 1992) at 1236.

1115, and *In re Wertheim*, 541 F.2d 257, 265, 191 U.S.P.Q. 90, 98 (CCPA 19769)."[2] Hence, the Appellant contends that, contrary to the Examiner's unsupported rejection, claims 72-105 are fully supported by the Specification under the correct standard.

The Examiner also argues:

> "The Claims further require instructions which translate data into recommendations for treatment option (claim 75), a display that can be printed (claim 77), instruction direct (sic) the fate of said data according to the subject's preference. None of these limitations are present in the instant application with regard to a computer program comprising instructions." (Final Office Action of May 10, 2005, page 4). (Emphasis added.)

The Examiner is wrong. Support for instructions which translate data into recommendations for treatment options (Claim 75) is found, for example, at page 50, line 19 – page 51, line 7 of the Specification:

> "The present invention contemplates any method capable of receiving, processing, and transmitting the information to and from medical personnel and subject. FIG. 2 illustrates the transformation of a sample (e.g., tissue sample or genetic information) into data useful for the clinician, subject or researcher. . . . Where the sample comprises previously determined genetic information (*e.g.*, sequence information, SNP or mutation information, etc.), the information may be directly sent to the genomic profiling service by the subject (*e.g.*, a information card containing the genetic information may be scanned by a computer and the data transmitted to a computer of the genomic profiling center using an electronic communication systems). Once received by the genomic profiling service, the sample is processed and a genomic profile is produced (*i.e.*, genomic data),

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[2] *All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 309 F.3d 774, 64 USPQ2d, 1945 (Fed. Cir. 2002).

specific for the medical or surgical procedure the subject will undergo. (Specification, page 50, line 19 – page 51 line 7.) (Emphasis added.)

And:

"The genomic profile data is then prepared in a format suitable for interpretation by a treating clinician. For example, rather than providing raw sequence data, the prepared format may represent a risk assessment for various treatment options the clinician may use or as recommendations for particular treatment options." (Specification, page 51, lines 8 – 11.) (Emphasis added.)

Similarly, page 50, lines 11 – 15 of the Specification teaches a display that can be printed (Claim 77):

"The data may be displayed to the clinician by any suitable method. For example, in some embodiments, the genomic profiling service generates a report that can be printed for the clinician (*e.g.*, at the point of care) or displayed to the clinician on a computer monitor." (Specification, page 50, lines 11 – 15.)

Similarly, page 52, lines 8 – 18 of the Specification teach instructions that direct the fate of the genomic data according to the subject's preference (Claim 82):

"Following the medical or surgical procedure, the subject's sample and the data generated by the genomic profile can follow one of several paths. The fate of the sample and the genomic data is driven by the subject, who is given a menu (*e.g.*, electronically) of choices. . . .In some embodiments, the subject may be able to directly access the data using the electronic communication system." (Specification, page 50 lines 8 – 18.) (Emphasis added.)

In the Final Office Action of May 10, 2005 the Examiner also argues:

"Claim 84 is directed to a computer program comprising instructions which direct a processor to analyze data to indicate an anesthesia treatment course of action. The specification does not appear to teach any computer program comprising instructions to indicate an anesthesia treatment course of action." (Final Office Action of May 10, 2005, page 4.))

The Examiner's rejection is groundless. For example, lines 8 – 17 of page 50 of the Specification teach:

"In some embodiments, a computer-based analysis program is used to translate the raw data generated by the genomic profile (*e.g.*, the presence or absence of a given SNP or mutation) into data of predictive value for the clinician (*e.g.*, probability of abnormal pharmacological response, presence of underlying disease, or differential diagnosis of known disease). The clinician (*e.g.*, surgeon or anesthesiologist) can access the predictive data using any suitable means. Thus, in some preferred embodiments, the present invention provides the further benefit that the clinician, who is not likely to be trained in genetics or molecular biology, need not understand the raw data of the genomic profile. The data is presented directly to the clinician in its most useful form." (Specification, page 50, lines 8 – 17.) (Emphasis added.)

And:

"In some embodiments, the course of action is administration of anesthesia during a surgical procedure; in other embodiments, the course of action is administration of anesthesia during a medical procedure. In some embodiments, the anesthesia is a general anesthesia. In other embodiments, the anesthesia is a regional anesthesia. In some embodiments, the surgical procedure is non-invasive surgery. In other embodiments, the surgical procedure is invasive surgery." (Specification, page 3, line 30 – page 4, line 6.) (Emphasis added.)

And:

"In some embodiments, the course of action is a surgical course of action; in other embodiments, the course of action is administration of anesthesia during a surgery." (Specification, page 5, lines 6 – 8.)(Emphasis added.)

And:

"In some embodiments, markers are included for additional underlying conditions that may influence the choice of anesthesia or other management." (Specification, page 38, lines 19 – 20.) (Emphasis added.)

The Examiner also argues:

"There are further no instructions to indicate dosages of compounds (claim 92-94), instructions for prophylaxis for thrombosis (claim 95), for example." (Final Office Action of May 10, 2005, page 4.) (Emphasis added.)

The Examiner is incorrect. For example, with regard to Claims 92-94 the Specification teaches:

"In some embodiments, markers for debrisoquine metabolism (*i.e.*, Cytochrome P450) defects are included in the perioperative genomic profile. Defects in the CYP2D6 gene known to disrupt the pharmacokinetics of certain drugs have been described (*See e.g.*, Sachse *et al.*, Am. J. Hum. Genet., 60:284 [1997]). . . . If a subject's predisposition to impaired or accelerated P450 metabolism is known, adverse drug reactions can easily be avoided by substituting other medications or adjusting dosages. (Specification, page 36, lines 13 - 20.) (Emphasis added.)

Similarly, with regard to Claim 95, the Specification teaches:

"In some embodiments, perioperative genomic profiles include markers for blood coagulations proteins or platelet deficiencies (*e.g.*, methylene tetrahydrofolate reductase, methionine synthase, cystathione β synthase, factor V Leiden, and prothrombin) known to increase or to decrease the risk of thrombosis (blood clots). . . . Prophylactic treatment (*e.g.*, anti-coagulation medications, positioning, and compression devices) and closer monitoring can reduce the incidence and severity of thrombus." (Specification, page 37, line 18 page 38, line 3.) (Emphasis added.)

In the Final Office Action of May 10, 2005, the Examiner alleges:

"The concept of "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents" does not appear to be part of the originally filed invention. Therefore, "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents" constitutes new matter. Applicant is required to cancel the new matter in reply to this Office Action." (Final Office Action of May 10, 2005, page 5.)

The Examiner is in error. To the contrary, the Specification teaches multiple examples of computer programs comprising instructions which direct a processor to analyze data including, for example, public databases that can be accessed only by computer (Specification, page 28, lines 25 – 29, and page 31, line 1 – page 32, line 15), and DNA chip assays (DNA microchips containing electronically captured probes, DNA arrays based on the segregation of fluids by differences in surface tension, and DNA bead arrays (Specification, page 43, line 24 – page 46, line 17), enzymatic methods of detection of hybridization (Specification, page 46, line 19 – page 48, line 2), and mass spectroscopy assays (Specification, page 48, line 4 – page 49, line 2). For example, with regard to the mass spectroscopy assay of page 49, lines 1 - 2 the Specification teaches:

"The SpectroTYPER software then calculates, records, compares and reports the genotypes at the rate of three seconds per sample."

Moreover, the Specification teaches computer programs "comprising instructions which direct a processor to analyze data derived from use of said reagents", for example, to acquire, transmit, analyze and distribute genomic data at page 51, lines 2 - 4:

> "an information card containing the genetic information may be scanned by a computer and the data transmitted to a computer of the genomic profiling center using an electronic communication system." (Emphasis added.)

And at Specification, page 51, lines 12 - 15:

> "For example, in some embodiments, the genomic profiling service generates a report that can be printed for the clinician (e.g., at the point of care) or displayed to the clinician on a computer monitor." (Emphasis added.)

And at Specification, page 51, lines 21 – 24:

> "The data generated by the assay may be converted to a genomic profile in a computer system of the emergency vehicle or may be transmitted to a distant computer system for processing." (Emphasis added.)

The Appellant asserts that, as an unmistakable matter of record, the Specification thoroughly supports Claims 72-105 that recite "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents". Nor can the Examiner ignore well-settled law that the claimed subject matter need not be described literally or *in ipsis verbis* in order for the Specification to satisfy the description requirement.[3] All that is necessary is that the application must reasonably convey the claimed subject matter to an artisan of ordinary skill.[4] In view of the above, the Appellant respectfully requests that the rejection be withdrawn.

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[3] *In re Lukach*, 442 F.2d 967, 969, 169 USPQ 795, 796 (CCPA 1971).
[4] *Ex parte Parks*, 30 USPQ 2d 1234 (B.P.A.I. 1994).

2. Claims 106 and 107 are Allowable, and Have Not Been Examined

In the Final Office Action of May 10, 2005 the Examiner argues:

> "Claims 72-107 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
>
> In the amended claims, reference to "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents" are (sic) included. The amendment fails to propose the basis for the new claim. Upon review by the examiner of support for the newly added recitation, the specification does not describe or discuss "a computer program comprising instructions which direct a processor to analyze data from use of said reagents." (Final Office Action of May 10, 2005, pages 2-3.)

The Examiner is wrong. Neither independent Claim 106, nor independent Claim 107, recite the element "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents". Therefore, the Appellant requests that these rejections be withdrawn.

3. The Specification Fully Supports the Subject Matter of Claims 72-107

Teachings in the Specification that describe the subject matter of Claims 72-107 are clear-cut, plentiful, and complete. As the evidence set forth above amply attests, the Examiner has misread the Specification. For these reasons the Appellant respectfully requests that the rejections be withdrawn.

B. Ground of Rejection 2 - Claims 72 – 107 Are Not Anticipated by the 1993 Applied Biosystems Product Catalog, pages 135-164.

1. The 1993 Applied Biosystems Product Catalog (pages 135-164) Does Not Teach Each and Every Element of Claims 72-107

In the Final Office Action of May 10, 2005 the Examiner argues:

"Claims 72-107 are rejected under 35 U.S.C. 102(b) as being anticipated by Applied Biosystems Product Catalog (1993, pages 135-164)." (Final Office Action of May 10, 2005, page 5.)

The Federal Circuit has stated the relevant analysis for anticipation as follows:

"A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference."[5]

The Appellant contends that the 1993 Applied Biosystems Product Catalog fails to teach each and every element of Claims 72 –107. Specifically, the 1993 Applied Biosystems Product Catalog fails to teach:

Claims 72, 84, and 101 - "reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are **sufficient** to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ* so as to generate a genomic profile for use in selecting a perioperative course of action for said subject" (Emphasis added.)

And:

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[5] *Verdegaal Bros. V. Union Oil of California*, 2 USPQ2d 1051, 1053 (Fed.Cir. 1987)

Claims 106 and 107 – "component parts configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are **sufficient** to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*" (Emphasis added.)

The Appellant emphasizes that the Examiner has ignored these claim elements entirely *i.e.*, reagents **sufficient** to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the specified group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*. None of the components of the Examiner's 1993 Applied Biosystems Product Catalog are specifically sufficient to detect the alleles of the present invention's claims. The Examiner has never pointed out where in the cited catalog these elements are to be found. It is a matter of simple fact the 1993 Applied Biosystems Product Catalog is insufficient, standing alone, to detect the alleles of the perioperative genomic profile kits of the present invention without more, *i.e*,. specific reagents to do so.

To the contrary, the 1993 Applied Biosystems Product Catalog does not mention in any way the genes *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ* of Claims 72-107. The 1993 Applied Biosystems Product Catalog does not teach the variant alleles in two or more of these genes of Claims 72-107 associated with two or more conditions (see, for example, Specification paragraphs [0135] "Applications and Interventions of Specific Markers" to [0149] "Genomic Profiling in Practice", and EXAMPLES 1 and 2). The 1993 Applied Biosystems Product Catalog does not teach reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject are **sufficient** to detect the presence or absence of the variant alleles of these genes of Claims 72, 84 and 101 (*e.g.*, Specification, EXAMPLES 1 and 2). And the 1993 Applied Biosystems Product Catalog does not teach component parts configured such that when exposed to a sample containing target

nucleic acid from a perioperative subject, are **sufficient** to detect the presence or absence of variant alleles in two or more genes of Claims 106 and 107 (*e.g.*, Specification, EXAMPLES 1 and 2).

The 1993 Applied Biosystems Product Catalog is a listing of general commercial reagents and products. Pages 135-164 of the 1993 Applied Biosystems Product Catalog provide the Applied Biosystems Model 373 electrophoresis unit and accessories, generic sequencing reagents (*e.g.*, polymerase, ddNTPs, buffers, dyes, controls and internal standards), template purification reagents, the Model 800 work station and accessories, and nucleic acid purification reagents. The Examiner does not argue that the catalog suggests using these reagents and components for perioperative applications, or for detection of the claimed genes and variant alleles. Rather, the Examiner is suggesting that, inherently, one or more of these reagents might find use as a component in such applications. However, in this analysis the Examiner entirely ignores claim elements of the present invention. None of the reagents or components of the 1993 Applied Biosystems Product Catalog, either singly or in combination, are **sufficient** to detect the presence or absence of the variant alleles of the genes of Claims 72, 84, 101, 106 and 107 when exposed to a sample containing target nucleic acid from a perioperative subject. Without more, *i.e.*, the claimed reagents of the present invention, the claimed detection of the present invention would not and cannot occur.

In the Final Office Action of May 10, 2005 the Examiner argues:

> "Applied Biosystems provides several products which are packaged for distribution, kits, which allow for detecting the presence of variant alleles of two or more genes. . . . Each of these products is capable of detecting the presence of variant alleles of two or more genes." (Final Office Action of May 19, 2005, page 6.)

In the Amendment and Response to Office Action filed February 17, 2005, the Appellant demonstrates to the Examiner that the Examiner's prior art does not teach the specific allele elements of the present claims. In the Final Office Action of May 10, 2005 the Examiner argues:

> "This argument has been reviewed but is not convincing because the claims recite "reagents which detect the presence of variant alleles of two or more genes . . ." This limitation does not require any allele specific elements. Reagents which detect the presence of variant alleles encompasses (sic) any product which may enable detection of variant alleles." (Final Office Action of May 10, 2005, page 7.)

Thus, the Examiner's position appears to be that the cited kits, when combined with other components not in the kit, might find use in detecting things. No attempt has been made be the Examiner to show that the cited kits contain components sufficient for the specific uses claimed.

The Examiner has erred by impermissibly neglecting claim limitations. The Examiner makes these rejections only by selectively glossing over explicit elements of Claims 72-107. The reason that the Examiner believes the limitation "does not appear to require any allele specific elements" is that the allele specific elements of the Claims have been edited out of the Examiner's quotation in the Final Office Action of May 10, 2005. The Examiner thereby overlooks succeeding and patentably distinct elements, *i.e.*, "reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject. . . are **sufficient** to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα and TNFβ.*" The Examiner has never indicated where these limitations are to be found in the 1993 Applied Biosystems Product Catalog. Nor has the Examiner ever responded to the Appellant's exhibit of these deficiencies in the Examiner's arguments.

Contrary to the Examiner's mischaracterizations, Claims 72-107 do not broadly encompass "ANY reagents capable of detecting the presence or absence of variant allele of two or more genes . . . " (Final Office Action of May 10, 2005, page 8.) (Emphasis in the original.). The term "ANY" is the Examiner's not the Appellant's. Nor are the Appellant's claims open-ended as the Examiner's repetitive use of ". . ." implies. The Appellant contends that it is improper for the Examiner to whittle away elements of the

claims, and then to reject the claims for lacking the elements the Examiner has carved off. Only by improperly revising the claims as paraphrased in the Final Office Action of May 10, 2005, and by mischaracterizing their scope, does the Examiner argue that the 1993 Applied Biosystems Product Catalog remotely anticipates the perioperative genomic profile kits of the present invention. To the contrary, Claims 72-107 explicitly recite reagents **sufficient** for allele specific detection of the genes *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα and TNFβ,* and the 1993 Applied Biosystems Product Catalog does not. For these reasons the Appellant respectfully requests that the rejections be withdrawn.

Nor are these the only elements missing from the 1993 Applied Biosystems Product Catalog. For example, the 1993 Applied Biosystems Product Catalog also fails to teach:

Claim 72 – a kit with reagents sufficient to generate "a genomic profile for use in selecting a perioperative course of action for a subject."

Claim 73 – "The kit of claim 72, wherein said instructions translate said data into information of predictive value for a clinician."

Claim 74 – "kit of claim 72, wherein said instructions translate said data into a risk assessment for treatment options."

Claim 75 – "The kit of claim 72, wherein said instructions translate said data into recommendations for treatment options."

Claim 76 – "The kit of claim 72, wherein said instructions generate a report for display to a clinician."

Claim 77 – "The kit of claim 76, wherein said display is in the form of a report that can be printed."

Claim 78 – "The kit of claim 76, wherein said display is in the form of a report on a computer monitor."

Claim 79 – "The kit of claim 72, wherein said instructions are sufficient to receive, process and transmit said data to and from said subject, a clinical laboratory and medical personnel."

Claim 80 – "The kit of claim 79, wherein said transmission of said data uses an electronic communication system."

Claim 81 – " The kit of 80, wherein said electronic communication system transmits said data to a distant computer system for processing."

Claim 82 – "The kit of claim 72, wherein said instructions direct the fate of said data according to said subject's preference."

Claim 83 – " The kit of Claim 72, wherein said instructions comprise information to optimize perioperative care that, based on at least the presence of variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*, directs a user to a specific perioperative clinical pathway for a subject.

Claim 84 – "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents to indicate an anesthesia treatment course of action.

Claim 85 – "The kit of Claim 84, wherein said instructions indicate a general anesthesia treatment course of action."

Claim 86 - "The kit of Claim 85, wherein said general anesthesia is an inhalational treatment course of action."

Claim 87 – "The kit of Claim 85, wherein said general anesthesia is an intravenous treatment course of action."

Claim 88 – "The kit of Claim 85, wherein said general anesthesia is a combined inhalational and intravenous treatment course of action."

Claim 89 – "The kit of Claim 84, wherein said instructions indicate a regional anesthesia treatment course of action."

Claim 90 – "The kit of Claim 84, wherein said instructions indicate a combined regional and general treatment course of action."

Claim 91 – "The kit of Claim 84, wherein said instructions indicate an anesthesia treatment course of action during a medical procedure."

Claim 92 – "The kit of Claim 84, wherein said instructions indicate dosages of analgesic compounds."

Claim 93 – "The kit of Claim 84, wherein said instructions indicate increasing the dosage of analgesic compounds metabolized by CYP2D6."

Claim 94 – "The kit of Claim 84, wherein said instructions indicate decreasing the dosage of analgesic compounds metabolized by CYP2D6."

Claim 95 – "The kit of Claim 84, wherein said instructions indicate prophylaxis for thrombosis."

Claim 96 – "The kit of Claim 84, wherein said instructions indicate increasing prophylaxis for thrombosis mediated by variant alleles of *F5, F2, MTHFR, MTR, MTRR,* and *CBS.*

Claim 97 – "The kit of Claim 84, wherein said instructions indicate decreasing prophylaxis for thrombosis mediated by variant alleles of *F5, F2, MTHFR, MTR, MTRR,* and *CBS.*

Claim 98 – "The kit of Claim 84, wherein said instructions indicate monitoring procedures."

Claim 99 – "The kit of Claim 84, wherein said instructions indicate pre-operative phenotypic tests and consultations."

Claim 100 – "The kit of Claim 84, wherein said instructions provide a prognosis after an anesthesia treatment course of action."

Claim 101 – "a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents to indicate a surgical treatment course of action."

Claim 102 – "The kit of Claim 101, wherein said instructions indicate a non-invasive surgery treatment course of action."

Claim 103 – "The kit of Claim 101, wherein said instructions indicate an invasive surgery treatment course of action."

Claim 104 – "The kit of Claim 101, wherein said instructions provide a prognosis after a surgical treatment course of action."

Claim 105 – "The kit of Claim 101, wherein said instructions indicate a post-operative treatment course of action."

Claim 106 – "a patient scheduled for a surgical procedure that has not yet completed said surgical procedure"

Claim 106 – "a genomic profile for use in selecting a perioperative course of action for a subject that directs a user to a specific clinical pathway of

medical intervention for said subject."

Claim 107 – "a genomic profile for use in selecting a perioperative course of action for a subject that directs a user to a specific clinical pathway of anesthesia intervention for said subject."

In the Final Office Action of May 10, 2005 the Examiner fails to divulge where in the 1993 Applied Biosystems Product Catalog the Examiner believes these missing elements of Claims 72-107 are to be found.

The Appellant contends that the 1993 Applied Biosystems Product Catalog does not describe the subject matter of Claims 72-107 of the present invention. This is because, prior to the filing date of the instant application, kits for generating the perioperative genomic profiles of the present invention were unknown to the skilled artisan, to the Patent and Trademark Office, and to the Examiner. For these reasons the Appellant respectfully requests that the rejections be withdrawn.

2. *In re Ngai* Stands for the Patentability of Claims 72 - 105

In rejecting Claims 72-107 under 35 U.S.C. §102(b) as being anticipated by pages 135-164 of the 1993 Applied Biosystems Product Catalog (Final Office Action of May 10, 2005 page 5) the Examiner has ignored the "instructions" element of the claims. The Appellant contends that the element is proper and cannot be ignored.

In the Final Office Action of May 10, 2005 the Examiner argues:

"As decided at the Federal Circuit in May 2004, In re Ngai succinctly states that inventors are "not entitled to patent a known product by simply attaching a set of instructions to that product." Whether the instructions are printed on a piece of paper within the kit, or the instructions are printed in the memory of the computer for execution, the instructions remain just instructions. With regard to claims 73-107, the intended use of the instructions written in the memory or program of the computer would not change the product. As in Ngai, the only difference between the Applied Biosystems system and the instant claims is the content of the

instructions. Therefore, the different instructions provided in Claims 73-107 do not distinguish over the prior art. Therefore, since Applied Biosystems teaches every limitation of the claims, Applied Biosystems anticipates the claimed invention." (Final Office Action of May 10, 2005, page 7.) (Emphasis in original.)

In *In re Ngai*, the inventor sought to patent a kit designed to perform the method recited in an earlier claim of the same patent application, i.e., claim 19 - "A kit for normalizing and amplifying an RNA population, said kit comprising instructions describing the method of claim 1". In distinguishing the facts of *In re Ngai* from the facts of its earlier holding in *In re Gulack*, the CAFC concludes:

> "In Gulack, the printed matter would not achieve its educational purposes without the band, and the band without the printed matter would similarly be unable to produce the desired result. Here, (*i.e.*, in *In re Ngai*) the printed matter in no way depends on the kit, and the kit does not depend on the printed matter. All that the printed matter does is teach a new use for an existing product. As the Gulack court pointed out, "where the printed matter is not functionally related to the substrate, the printed matter will not distinguish the prior art in terms of patentability." If we were to adopt Ngai's position, anyone could continue patenting a product indefinitely provided that they add a new instruction sheet to the product. This was not envisioned by Gulack. Ngai is entitled to patent his invention of a new RNA extraction method, and the claims covering that invention were properly allowed. He is not, however, entitled to patent a known product by simply attaching a set of instructions to that product." (*In re Ngai*, 367 F.3d 1336, 1340.) (Emphasis added.)

Thus, in *In re Gulack* and *In re Ngai* the CAFC establishes a two-pronged test. If the product sought to be patented is:

1.) previously unknown, and/or

2.) the printed matter is functionally related to the substrate

then the product is expressly entitled to a patent (*In re Gulack*). If, on the other hand, the product is previously known, and the printed matter is not functionally related to the substrate, then the product is not entitled to a patent (*In re Ngai*). In failing to recognize these distinctions, and their direct application to the facts of the present invention, the Examiner has made a number of errors.

a. Claims 106 and 107 are Allowable, and Have Not Been Examined

Although the Examiner has rejected Claims 106 and 107, the Examiner has misread the Claims. Contrary to the Examiner's misapprehension, Claims 106 and 107 do not teach "instructions printed on a piece of paper", "instructions printed in the memory of a computer for execution", or instructions "printed in the program of the computer." Therefore, the Examiner's rejections of Claims 106 and 107 are in error. For these reasons the Appellant respectfully requests that the Board withdraw the Examiner's rejections of Claims 106 and 107.

b. The Perioperative Genomic Profile Kits of the Present Invention Are Not an Existing Product

The Examiner's rejection of Claims 72-107 leans on a single reference in support of the Examiner's speculation that the perioperative genomic profiling kits of the present invention are an existing product that is previously known, *i.e.*, the 1993 Applied Biosystems Product Catalog. To the contrary, as detailed in Section VIII.B.1. of the present Brief (see above, pages 23 - 30), the 1993 Applied Biosystems Product Catalog lacks multiple elements of Claims 72-107. For example, the 1993 Applied Biosystems Product Catalog fails to teach the reagents of Claims 72, 84 and 101, and fails to teach the component parts of Claims 106 and 107. Nor does the 1993 Applied Biosystems Product Catalog teach, for example, the computer based program that translates data into information of predictive value for a clinician of Claim 73, the electronic communication

system of Claim 80, the specific perioperative clinical pathway of Claim 83, the anesthesia treatment course of action of Claim 84, or the surgical treatment course of action of Claim 101. By overlooking the many factual differences between the 1993 Applied Biosystems Product Catalog and Claims 72-107 of the present invention, the Examiner mistakenly alleges that the perioperative genomic profile kits of the present invention are previously known. However, the Examiner has never revealed where in the 1993 Applied Biosystems Product Catalog these and other (see above) missing elements are to be found. Because the genomic profiling kits of the present invention are not an existing product, and are not previously known, the Examiner is in clear error.

The Examiner argues:

> "Since the facts and analysis of the instant application and Ngai are the same, Ngai is deemed the closest authority on the issue of whether printed instructions in a previously disclosed kit makes the kit patentable." (Final Office Action of May 10, 2005, page 8.)

To the contrary, as the Appellant has demonstrated, the facts and analysis of the instant application and Ngai are not the same, and therefore the Claims 72-107 of the present invention directly fulfill the first prong of the *In re Ngai* test. For these reasons the Appellant respectfully requests that the Board withdraw the Examiner's rejections of Claims 72-107.

c. The Computer Programs of Claims 72-105 Are Functionally Related To The Kits Of The Present Invention

In the Amendment and Response to Office Action filed February 17, 2005, the Appellant pointed out to the Examiner that:

> "The instructions of the present invention are new, unobvious and functionally related to the substrate kit. Instructions and reagents of the present invention are interrelated, so as to produce a new product useful for the purpose of

generating a perioperative genomic profile for a subject. Instructions of the present invention do not achieve their purpose of generating a perioperative genomic profile without the reagents, and the reagents of the present invention do not produce the desired result without instructions." (Amendment and Response to Office Action filed February 17, 2005, page 12.) (Emphasis added.)

In the Final Office Action of May 10, 2005 the Examiner fails to respond in answer to these facts in any manner whatsoever. The Examiner has never taken issue with the fact that the computer programs comprising instructions of the present invention are functionally related to the kits of Claims 72-105. Indeed, the Examiner's statement that "instructions are printed in the memory of the computer for execution" (Final Office Action of May 19, 2005, page 7) explicitly acknowledges the functional relationship of component computer programs and elements of the kits of Claims 72-105.

On the other hand, the Appellant has provided evidence of the functional relationship between the instructions of the present claims and their substrate kits in the form of the Declaration of Dr. Morris Waxler, dated September 8, 2003. In this Declaration, an expert explains that it is a matter of fact that instructions for the use of an *in vitro* genetic diagnostic kit bear a critical functional relationship to the components of the kit, and that the function of an *in vitro* genetic diagnostic kit depends on the instructions.

"The function of an *in vitro* genetic diagnostic kit depends on the instructions to be approved by the Food &Drug Administration; without instructions the *in vitro* genetic diagnostic kit is not considered to be functional by the Food & Drug Administration."

"an *in vitro* genetic diagnostic kit does not, and cannot, function equally effectively with or without instructions."

"The functional relationship between an *in vitro* genetic diagnostic kit and its operation is critical such that component instructions must undergo rigorous

> Food & Drug Administration scrutiny before the kit may be manufactured or marketed in order to assure its safety, efficacy and reliability."
>
> "Without Food & Drug Administration approved instructions for its operation an *in vitro* genetic diagnostic kit cannot be manufactured or marketed." (Declaration of Morris Waxler, Ph.D. under 37 CFR §1.132, page 1)

Hence, the Declaration of Dr. Waxler is objective, factual evidence of a functional relationship between instructions of the present invention that enable use of the reagents, and instructions for the use of data obtained by use of the reagents in the hands of practitioners.

In the Final Office Action of May 10, 2005 the Examiner fails to respond to these facts. Instead of addressing the content of Dr. Waxler's Declaration, the Examiner completely dodges the functional relationship issue. The Examiner argues:

> "Moreover the Declaration of Morris Waxler has been thoroughly considered and deemed not persuasive. The Declaration is specifically designed to establish that instructions for kits, for the purpose of the FDA, are considered functional by the FDA. This argument has been thoroughly reviewed, but is not found persuasive because the standard to patentability does not rely on any requirements made by the FDA. As provided in MPEP 2107.10, for example, it is clear that the requirements for FDA and patent approval should not be confused. Thus it is clear that the requirements for the FDA approval and for patent approval are not parallel and conclusions regarding FDA requirements are not persuasive of binding on the patent process. Further, as argued in the February 14, 2005 response, page 14, the response correctly points out that the only reference to the FDA addresses therapeutic utility. It is clear based upon the silence of the MPEP with regard to the FDA on instructions and kits, that the FDA approval process is not considered in the distinct patenting process." (Final Office Action of May 10, 2005, page 10.) (Emphasis added.)

In reviewing the Declaration of Dr. Morris Waxler the Examiner makes a number of errors. First, the Examiner's response fails to discuss, consider or even mention the matter in

question, *i.e.*, the functional relationship between the computer programs comprising instructions and the kits of Claims 72-107. The claimed instructions of the present invention clearly result in structural and manipulative differences between the 1993 Applied Biosystems Product Catalog cited by the Examiner as prior art, and the articles and compositions of the present claims. Rather than remaining fully functional, the useful, concrete, and tangible aspects of the kits of the present claims are not maintained after removal of the claimed computer programs.

Second, the only reference to the FDA in MPEP 2107.01 addresses therapeutic utility, stating that standards for patentability are legitimately lower than standards for FDA approval for safety and efficacy of pharmaceutical inventions ("FDA approval is not a prerequisite for finding a compound useful within the meaning of the patent laws.") To the contrary, the Appellant has pointed out to the Examiner that the present invention is not a pharmaceutical invention.

Third, the MPEP 2107.01 manifests no guidance for appraising the presence or absence of a functional relationship between novel and unobvious instructions and an unknown product. As well, the CAFC asserts, and the MPEP confirms, that a patent may issue despite failing to meet the higher FDA barrier, the exact opposite circumstance of the present disclosure. Finally, "the silence of the MPEP with regard to the FDA on instructions and kits" does not excuse the Examiner from fulfilling the Patent and Trademark Office's duty in determining the presence or absence of a functional relationship as the CAFC has instructed in *In re Gulack* and *In re Ngai.*

The Examiner has presented no evidence in support of the lack of a functional relationship between the claimed instructions and other components of the kits of Claims 72-105, or in contradiction to Dr. Waxler's Declaration. The Examiner's rejection standing alone is not evidence. The Examiner's citation of MPEP 2107.01 fails to remedy this deficiency, nor is the Examiner in possession of countervailing factual evidence. Indeed, in the Final Office Action of May 10, 2005, the Examiner does not argue the functional relationship between the computer programs comprising instructions of Claims 72-105 and other kit components, and thereby concedes the issue. For these reasons the Appellant respectfully requests that the Board withdraw the Examiner's rejections of Claims 72-105.

d. The Computer Programs of Claims 72-105 Are Not Printed Matter

In the Final Office Action of May 10, 2005 the Examiner argues with reference to *In re Ngai*:

> "Whether the instructions are printed on a piece of paper within the kit, or the instructions are printed in the memory of the computer for execution, the instructions remain just instructions." (Page 7.) (Emphasis added.)

Contrary to the Examiner's misinterpretation, *In re Ngai* does not address, consider or even mention computers, computer programs, computer programs comprising instructions, or computer analysis of data. Specifically, *In re Ngai* does not hold that instructions "printed on a piece of paper" are identical to "instructions printed in the memory of the computer for execution." This assertion, which represents new law and is the Examiner's conclusion alone, is unsupported in the Final Office Action of May 10, 2005 by evidence, PTO Guidelines, statute or CAFC holdings.

Indeed, if the Examiner's assertion were valid, it would contradict decades of case law holding that software is patentable. For example, *In re Beauregard*, 53 F.3d 1583, 35 USPQ2d 1383 (Fed. Cir. 1995) states:

> "The Board rejected Beauregard's computer program product claims on the basis of the printed matter doctrine. Beauregard appealed. The Commissioner now states 'that computer programs embodied in a tangible medium, such as floppy diskettes, are patentable subject matter under 35 U.S.C. §101 and must be examined under 35 U.S.C. §§ 102 and 103'. The Commissioner states that he agrees with Beauregard's position on appeal that the printed matter doctrine is not applicable." *In re Beauregard*, 53 F.3d 1583, 1584.

Similarly, the "computer program comprising instructions which direct a processor to analyze data derived from use of said reagents" of Claims 72, 84 and 101 is fully in accord with the Patent and Trademark Office's "Examination Guidelines for

Computer –Implemented Inventions" which states:

> "a claimed computer readable medium encoded with a data structure defines structural and functional interrelationships between the data structure and the medium which permit the data structure's functionality to be realized and is thus statutory." (Patent and Trademark Office, Examination Guidelines for Computer-Related Inventions, 61 Fed. Reg. 7478 (Feb. 28, 1996), 7481-7482.)

> And:

> "a computer-readable medium encoded with a computer program defines structural and functional interrelationships between the computer program and the medium which permit the computer program's functionality to be realized, and is thus statutory." (Patent and Trademark Office, Examination Guidelines for Computer-Related Inventions, 61 Fed. Reg. 7478 (Feb. 28, 1996), 7481-7482.)

Hence, computer instructions which direct a processor to analyze data for generating a perioperative genomic profile for a subject as claimed, qualify as statutory subject matter because storage of the computer instructions turns a computer readable medium into a functional component which directly cooperates with the processor. Computer instructions cause computer functions to occur, and are therefore inarguably functional components of the computer system. Unquestionably, Claims 72, 84 and 101 recite "a computer program" comprising "instructions", "a processor", and data structures derived from the use of claimed reagents. The Examiner has never disputed the presence of these elements in the Claims, nor has the Examiner argued their lack of functional inter-relationships. For these reasons, the Examiner's arguments do not support a rejection.

As the Appellant has pointed out to the Examiner, instructions taught by Claims 72-105 are novel, physical components of the kits of the present invention that dictate the manipulations of physical objects and activities that, as components of the claimed kits, implement a set of actions to accomplish a useful, concrete and tangible result.

(Amendment and Response to Office Action filed February 17, 2005, page 13.). In the Final Office Action of May 10, 2005 the Examiner fails to rebut, or even address, these facts.

The claimed and patentable computer programs comprising instructions for operation of the present invention embody functional components that interact with other components of the claimed kits in novel modes of cooperation, thereby permitting the kit's functionality to be realized. Hence, the computer programs comprising instructions of Claims 72-105 are physical component parts of the Claims. A Claim that recites "A system comprising component Y and component Z, wherein component Z is configured to permit component Y to find use in process X" is patentable if the prior art does not teach the use of component Y in process X, or does not teach the use of component Z that is configured to facilitate the use of Y for X. The instructions of the present invention direct, for example, a treatment course of action utilizing physically organized data structures for two or more assays that are not fixed or determinate beforehand. Thus, a subject's preferred clinical pathway cannot properly be executed in advance, absent the results of the assay as instructed. Instructions that cause and direct a particular treatment course of action utilize results from two or more genotypes. A combination of variant alleles may well instruct one course of action rather than another. Although these facts have been specifically set forth in the Amendment and Response of Office Action filed February 17, 2005 (page 13), in the Final Office Action of May 10, 2005, the Examiner has been mute in response.

e. The Examiner's Novel "Useful for Other Purpose" and "Physically Affect the Chemical Nature" Standards of Anticipation Are Not the Law Under 35 U.S.C. 102(b)

In the Final Office Action of May 10, 2005 the Examiner argues:

"With respect to the arguments (page 16-17) of the response filed on June 30, 2004 and February 14, 2005, the response argues that "physically or chemically affect the chemical nature" and "uses for other purpose" is not the law. This argument has been

thoroughly reviewed, but is not found persuasive because it is clear from the decision of Ngai that since the known products are not changed, the inventor can not patent kits simply by attaching new set of instructions to that product." (Final Office Action of May 10, 2005, pages 10-11).

The Examiner is mistaken with regard to a number of facts. First, *In re Ngai* makes no mention of either of the Examiner's improper standards proposed by the Examiner for testing the validity or invalidity of novel, unobvious instructions by anticipation under 35 U.S.C. 102(b). Nor in the Final Office Action of May 10, 2005 has the Examiner brought forward support in any citation to relevant case law, the MPEP, an affidavit, or other authority for these standards in which the legal test for a functional relationship between instructions and a substrate rests on whether operational instructions "physically or chemically affect the chemical nature of the components of the kit", or whether components of the kit are "useful for other purposes", as requested by the Appellant in the response filed on February 17, 2005 (page 16). The Examiner's standards are non-legal and innovative rules that the Examiner has made up, and do not comport with the law. Nor has the Examiner addressed these facts in the Final Office Action of May 10, 2005.

Second, as detailed above, the products of the present invention (*i.e.*, kits for generating a perioperative genomic profile for a subject), are not previously known or existing. Third, the products of the present invention (kits for generating a perioperative genomic profile for a subject), are specifically changed by the claimed computer programs comprising instructions. Fourth, in the response filed February 17, 2005, the Appellant directed the Examiner to abundant examples in the Specification of the present invention of instructions that both chemically and physically affect the chemical nature of the components of the kit (See Section I.B. "Criteria for Selection of Markers", page 32, Section I.C. "Categories of Markers", page 34, Experimental Example 1 "Perioperative Genomic Screening for Anesthesia Markers", page 53, Experimental Example 2 "Generation of Genomic Profiles", page 57). The Examiner has not responded to these citations in the Final Office Action of May 10, 2005. Therefore, the Appellant requests that these rejections be withdrawn.

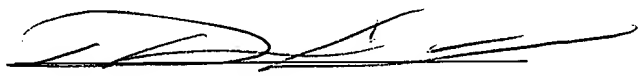
3. Claims 72 – 107 Are Not Anticipated under 35 U.S.C. 102(b) by the 1993 Applied Biosystems Product Catalog, pages 135-164

As detailed above, the 1993 Applied Biosystems Product Catalog fails to teach each and every element of Claims 72-107. In turn, the kits for generating the perioperative genomic profiles of the present invention were unknown to the skilled artisan, to the Patent and Trademark Office, and to the Examiner prior to the filing date of the present invention. Because the kits of Claims 72-107 are previously unknown, and because the Examiner has never disputed the functional relationship between the computer based instructions and kit components of the present invention, *In re Ngai* stands in direct support of the patentability of Claims 72-105 to the extent that the holding with regard to printed matter is relevant to computer programs comprising instructions which direct a processor to analyze data. (The Appellant notes that the CAFC's holding in *In re Ngai* is directed to printed matter, and not to computer-based data analysis programs.) Moreover, the Appellant contends that the Examiner has failed to examine Claims 106 and 107 that lack a computer program comprising instructions as claim elements. For these reasons the Appellant requests that the Board withdraw the Examiner's rejections.

C. CONCLUSION

For the foregoing reasons, it is submitted that the Examiner's rejection of Claims 72-107 was erroneous, and reversal of the rejection is respectfully requested. The Appellant requests that the Board render a decision as to the allowability of the Claims.

Dated: 11/7/05



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VIII. CLAIMS APPENDIX

I claim:

Claims 1 - 71 (cancelled).

72. (previously presented) A kit for generating a perioperative genomic profile for a subject, comprising:

a) reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β so as to generate a genomic profile for use in selecting a perioperative course of action for said subject; and

b) a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents.

73. (previously presented) The kit of claim 72, wherein said instructions translate said data into information of predictive value for a clinician.

74. (previously presented) The kit of claim 72, wherein said instructions translate said data into a risk assessment for treatment options.

75. (previously presented) The kit of claim 72, wherein said instructions translate said data into recommendations for treatment options.

76. (previously presented) The kit of claim 72, wherein said instructions generate a report for display to a clinician.

77. (previously presented) The kit of claim 76, wherein said display is in the form of a report that can be printed.

78. (previously presented) The kit of claim 76, wherein said display is in the form of a report on a computer monitor.

79. (previously presented) The kit of claim 72, wherein said instructions are sufficient to receive, process and transmit said data to and from said subject, a clinical laboratory and medical personnel.

80. (currently amended) The kit of claim 73, wherein said transmission of said data uses an electronic communication system.

81. (currently amended) The kit of claim 74, wherein said electronic communication system transmits said data to a distant computer system for processing.

82. (previously presented) The kit of claim 72, wherein said instructions direct the fate of said data according to said subject's preference.

83. (previously presented) The kit of Claim 72, wherein said instructions comprise information to optimize perioperative care that, based on at least the presence of variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β, directs a user to a specific perioperative clinical pathway for said subject.

84. (previously presented) A kit for generating a perioperative genomic profile for a subject, comprising:

a) reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β so as to generate a genomic profile for use in selecting a perioperative course of action for said subject; and

b) a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents to indicate an anesthesia treatment course of action.

85. (currently amended) The kit of Claim 84, wherein said instructions indicate an a general anesthesia treatment course of action.

86. (previously presented) The kit of Claim 85, wherein said general anesthesia is an inhalational treatment course of action.

87. (previously presented) The kit of Claim 85, wherein said general anesthesia is an intravenous treatment course of action.

88. (previously presented) The kit of Claim 85, wherein said general anesthesia is a combined inhalational and intravenous treatment course of action.

89. (currently amended) The kit of Claim 84, wherein said instructions indicate an a regional anesthesia treatment course of action.

90. (previously presented) The kit of Claim 84, wherein said instructions indicate a combined regional and general treatment course of action.

91. (previously presented) The kit of Claim 84, wherein said instructions indicate an anesthesia treatment course of action during a medical procedure.

92. (previously presented) The kit of Claim 84, wherein said instructions indicate dosages of analgesic compounds.

93. (previously presented) The kit of Claim 84, wherein said instructions indicate increasing the dosage of analgesic compounds metabolized by CYP2D6.

94. (previously presented) The kit of Claim 84, wherein said instructions indicate decreasing the dosage of analgesic compounds metabolized by CYP2D6.

95. (previously presented) The kit of Claim 84, wherein said instructions indicate prophylaxis for thrombosis.

96. (previously presented) The kit of Claim 84, wherein said instructions indicate increasing prophylaxis for thrombosis mediated by variant alleles of *F5, F2, MTHFR, MTR, MTRR,* and *CBS.*

97. (previously presented) The kit of Claim 84, wherein said instructions indicate decreasing prophylaxis for thrombosis mediated by variant alleles of *F5, F2, MTHFR, MTR, MTRR,* and *CBS.*

98. (previously presented) The kit of Claim 84, wherein said instructions indicate monitoring procedures.

99. (previously presented) The kit of Claim 84, wherein said instructions indicate pre-operative phenotypic tests and consultations.

100. (previously presented) The kit of Claim 84, wherein said instructions provide a prognosis after an anesthesia treatment course of action.

101. (previously presented) A kit for generating a perioperative genomic profile for a subject, comprising:

a) reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β so as to generate a genomic profile for use in selecting a perioperative course of action for said subject; and

b) a computer program comprising instructions which direct a processor to analyze data derived from use of said reagents to indicate a surgical treatment course of action.

102. (previously presented) The kit of Claim 101, wherein said instructions indicate a non-invasive surgery treatment course of action.

103. (previously presented) The kit of Claim 101, wherein said instructions indicate an invasive surgery treatment course of action.

104. (previously presented) The kit of Claim 101, wherein said instructions provide a prognosis after a surgical treatment course of action.

105. (new) The kit of Claim 101, wherein said instructions indicate a post-operative treatment course of action.

106. (previously presented) A perioperative genomic profile kit having component parts configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical

procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*, so as to generate a genomic profile for use in selecting a perioperative course of action for said subject and thereby providing a subject-specific clinical pathway for said subject, comprising information to optimize perioperative care that, based at least on the presence or absence of said variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ* measured by said kit, directs a user to a specific clinical pathway of medical intervention for said subject.

107. (previously presented) A perioperative genomic profile kit having component parts configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ*, so as to generate a genomic profile for use in selecting a perioperative course of action for said subject and thereby providing a subject-specific clinical pathway for said subject, comprising information to optimize perioperative care that, based at least on the presence or absence of said variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNFα* and *TNFβ* measured by said kit, directs a user to a specific clinical pathway of anesthesia intervention for said subject.

IX. EVIDENCE APPENDIX

A Declaration filed on September 8, 2003 is of record.

X. RELATED PROCEEDINGS APPENDIX

No decisions have been rendered by a court or the Board in any proceeding identified pursuant to paragraph (c)(1)(ii) C.F.R. §41.37